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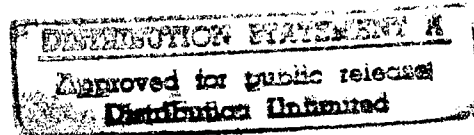
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USSR

[Translation]

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CONCEPTS ON THE ORIGIN OF CANCER AND OTHER TRUE TUMORS

(USSR)

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True tumors, blastomas, are one of the most extensive manifestations of pathological life. We find them with a striking similarity in many species of animals and even in plants. Widely varied physical, chemical and biological factors, both internal (nervous and hormonal) and external (parasitic), can lead to the appearance of blastomas.

Is our actual knowledge of the appearance and growth of true tumors sufficient for it to be brought together fruitfully in a dialectic interpretation? Of course, our knowledge is still far from sufficient for composing an exhaustive theory of the appearance and growth of true tumors. However, we believe that at this stage the principal lines of dialectic materialism can be applied with benefit for comprehension and prognosis (two key factors of any science) to our observations of the appearance and growth of true tumors.

Starting with the law of dialectic materialism that there is a universal relationship between natural phenomena, we may say that the growth of tumors is closely related to normal growth and to deviations from normal. These deviations may be in the form of malformations or of so-called benign tumors, which frequently make a difficult-to-catch transition to malignant forms. From this we may conclude that benign and malignant growths are not something foreign to the organism or accidentally thrust on the organism from the outside. On the contrary, it is something inherent that manifests itself under the effect of various internal and external factors. This circumstance helps us to understand a statement of L. Dmukhovskiy, a prominent expert of modern oncology, in which he says that cancer, being a phenomenon depending on many factors, is related to physiological processes to a lesser or greater degree.

Going on to the principal law of dialectic materialism concerning the emergence of qualitative changes by means of a quantitative preparation, culminating in a spasmodic revolution, it is easy to see that blastomatous

growth appears in the cells as a new property, occurring suddenly as a result of a transition from quantitative changes into qualitative. It was the general practice to designate these changes as a "malignant mutation," a malignant variation of cells (when we still had in mind malignant tumors only).

Various relatively specific factors (by no means all and not always identical), such as mechanical, physical, chemical, actinic and biological effects of the environment, react in an appropriate way on metabolism. They create in one or another tissue or cell of the organism quantitative changes, which increase gradually and slowly. Having reached a critical point, these changes suddenly assume a new quality, which is the capacity to grow without termination (blastomatous growth). This is the tumofacient variation, which changes sharply the properties of the cells. The nature of this transformation is far from explored. One may probably assume that it is related to the peculiarities of cellular fermentative properties which acquire tumofacient properties.

We shall leave aside the question of differentiation and of morphological and chemical characteristics of tumors for they do not give us a true picture of the distinctive marks of tumoral cells compared with the normal ones of a living organism or of tissue culture outside the organism. However, these characteristics brought all pathologists, who study the phenomena objectively, to the idea that tumoral cells develop from normal ones.

In analyzing the results of observations and experiments here and abroad on the origin and growth of benign and malignant tumors, we are bound to conclude that biological characteristics of tumor growth are very significant. Indeed, even the most benign tumors, such as lipomas, grow at the expense of the surrounding tissues; they grow and increase in weight even when the body weight decreases, losing its normal reserves of fat under the effect of some cause. Some so-called benign tumors: myomas, fibroepithelial tumors, cystomas and even lipomas, can reach enormous sizes, progressively exhausting the carrier's organism. It goes without saying that malignant tumors, cancer and sarcoma, develop luxuriantly at the expense of the body parts which they destroy and exhaust totally until death.

Generally known characteristics of the growth of tumoral tissues can hardly be considered as anything other than ways of recognizing that tumoral tissues and cells have peculiar mechanisms of growth unfamiliar to normal tissues and cells. Their growth is controlled in the organism to a much lesser degree than that of the normal tissues. Can we think that the origin of these peculiar mechanisms of tumoral growth appears autogenously, independently, in the cells irrespective of the influence of their environment? Of course not. The whole

experience of oncology indicates that it is precisely the effects of environment, particularly chemical and actinic, that produce a tumofacient and malignant mutation of cells. Once the effect of environment has been assimilated by the cells, they become tumoral. Then the vigor of their progressive development is determined by the cells themselves to a much greater degree than by the surrounding systems and cells of the organism. The systems and cells of the organism injured to a greater or lesser degree do not participate in the tumor's growth.

Indeed, we know that, first of all, the growth of many tumors is not confined to the immediate encirclement of normal tissues of the organism. On the contrary, metastases transferred to new, sometimes distant areas, always develop there by multiplying their own cells and not by transforming the cells of the normal surrounding tissues. Secondly, if the original tumoral site is radically exsected or destroyed in good time, then, in many cases, the organism recovers and no new tumors occur. If some cells are left behind, then a further growth of tumors occurs almost without fail until the disease-ridden organism dies. Thirdly, many forms of malignant tumors, removed from animal organisms and transferred in the form of small strips or even of a single cancerous cell to a culture medium suitable for their growth, can start growing energetically. After passing through a number of culture media outside the organism, they preserve their inherent characteristics of aggressive growth. They obviously manifest these characteristics when replanted in the organism of the same animal species. Finally, in the fourth place, in inducing tumors by any cause originating in the environment (such as radiation or chemical substances), an instant occurs when there is still no tumor but discontinuation of the irritation will not prevent any longer the impending tumofacient mutation, blastomatosis. This means that it had potentially occurred, that some normal cells had already adopted tumofacient characteristics and, in this way, acquired their blastomatous mechanisms of growth and multiplication.

These well-known facts make us recognize that the leading factor of tumor growth, starting from the moment when the cells acquire blastomatous properties, lies not outside the cells of tumor but in them. Tumoral cells have their own mechanisms or, as it is generally said in oncology, autonomy. They are "allonomous," i.e., growth characteristics subject to other laws. Does it mean that tumors developing in the organism are independent of its influences and that the nervous or endocrine systems do not produce or cannot produce a slowing down, retaining or accelerated effect on tumor's growth? Of course not. The question is not of independence but only of allonomy (from Greek allos-other and nomos-law), i.e., a growth controlled by other laws. In recent years, examples of a very obvious hormonal effect produced on tumor's growth continuously

increased. For instance, it is widely known that sexual hormones have a certain effect on cancer growth of the prostate and breast. The effect of the pituitary and adrenal glands on the growth of certain tumors in sexual and breast glands is also generally known.

The concept of tumoral autonomy has recently met with opposition from some of the oncologists and representatives of general biology. But this opposition is legal only as long as the precise definition of the term autonomy in relation to tumor's growth remains little known. We consider that the concept of allonomy is fully applicable to tumor's growth and that the concept of autonomy (independence) from the organism is not all applicable. In our opinion, the concept of autogenesis, i.e., emergence on its own initiative, is still less applicable as the causes of tumor's origin lie not in the normal cells but in the interaction of these cells with the environment conditions. Normal cells become tumoral only after assimilating these conditions. From that moment they become allonomous, subject to other laws, although they are completely independent from the carrier's organism.

Therefore, we must at the present time have a clear idea that tumor's growth represents an allonomous process, subject to special mechanisms different from those of the normal cells and that the term autonomy is used only conventionally from an established practice.

Further, we should gradually approach the theoretical concept of the nature of this process. To do this, we must critically examine the concept of tumofacient "mutation."

The term "mutation" stands for a sudden resistant variation occurring in the morphological and biological properties of the organism or cells and which is transmitted to their progeny. This phenomenon was thoroughly explored by de Vries about 60 years ago in plants. However, it was already observed more than 100 years ago by Geoffroy Saint-Hilaire and more than 90 years ago by Darwin. De Vries attempted to explain by mutations the process of evolution as a natural, autogenetic property of the organism, i.e., properties independent of environmental effect. The mechanism of mutation was at first unexplained, then it was connected with the changes of the chromosomes and genes only. The Morgan school of thought followed this line in experiments on *Drosophila* fly.

The phenomenon of sudden biological variation and the possibility of reproducing it in experiments by irradiating embryos or lower organisms, such as yeast, must be considered firmly established. But the so-called mutation theory of evolution put forward by de Vries, isolating the organism from the environment, appears to us as anti-biological and inadmissible as the solely hereditary chromosomic theory.

Tumofacient mutation as the origin of tumor growth has apparently been debated since the twenties of our century and then chiefly as a malignant transformation which occurs more frequently in somatic cells than in embryonic.

Any oncologist is well informed that the emergence of many tumors in man, developing suddenly with cellular sites growing progressively, is preceded by dystrophic and chronically inflammatory manifestations over a long period of time. Experimental workers have also observed very similar manifestations in animals with induced malignant tumors.

Sufficiently numerous observations confirm that tumoral cells are governed by mechanisms different from normal cells. Thus, it was discovered that malignant cells can adapt themselves to growing in foreign organisms better than normal cells, providing necessary conditions are created for this adaptation. G. Roskin, Soviet histologist, already in the twenties of our century grew with success human cancerous cells in the anterior chamber of rabbit's eye. Green and Murphy, American biologists, already in the forties were able to demonstrate that chicken's sarcoma could be grown not only in the optic tissues but also in other organs of mammary animals.

Contradictions of the existence of biological malignant transformations in the cells are not convincing. This transformation varies only some of the properties of the organism, tissues and cells and not all. For this reason, some secretory functions preserved in tumors and ability to differentiate do not refute the theory that tumors originate from a sudden biological variation. This thesis does not conform at all with de Vries' theory of mutation evolution mentioned above and does not indicate in any way that malignancy is accidental, which would be contrary to the entire experience of experimental oncology.

The mechanism of tumofacient transformation is still not very clear. In particular, we do not have sufficient material on vertebrate animals and human beings to relate "mutations" to the changes occurring in the chromosomes only and may fully think that these changes occur in any other parts or molecules of the cells actively participating in multiplication. For this reason, we do not object to A. M. Magat's proposal of writing the word "mutation" in parenthesis or to accompanying the word with the adjective "malignant." We are even prepared to repudiate entirely the word "mutation" in oncology and to replace it with that of "tumofacient variation" (but not degeneration) of cells. The matter can only profit by this replacement of term because there will be less reason to unite into one the concepts of tumofacient mutation and of chromosomic and genetic mutation, the latter is so designated by geneticists of the Morgan school of thought.